

SUBSTITUTE SEQUENCE LISTING

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 Protein Design Labs, Inc.

<120> Humanized Antibodies To Gamma-Interferon

<130> 011823-008110US

<140> 09/450,520

<141> 1999-11-29

<150> 60/110,523

<151> 1998-12-01

<160> 13

<170> PatentIn Ver. 2.1

<210> 1

<211> 381

<212> DNA

<213> Mus spp.

<220>

<221> CDS

<222> (1)..(381)

<223> AF2 VL

<400> 1

atg gaa tca cag act ctg gtc ttc ata tcc ata ctg ctc tgg tta tat	48		
Met Glu Ser Gln Thr Leu Val Phe Ile Ser Ile Leu Leu Trp Leu Tyr			
1	5	10	15

ggt gct gat ggg aac att gtt atg acc caa tct ccc aaa tcc atg tac	96		
Gly Ala Asp Gly Asn Ile Val Met Thr Gln Ser Pro Lys Ser Met Tyr			
20	25	30	

gtg tca ata gga gag agg gtc acc ttg agc tgc aag gcc agt gaa aat	144		
Val Ser Ile Gly Glu Arg Val Thr Leu Ser Cys Lys Ala Ser Glu Asn			
35	40	45	

gtg gat act tat gta tcc tgg tat caa cag aaa cca gag cag tct cct	192		
Val Asp Thr Tyr Val Ser Trp Tyr Gln Gln Lys Pro Glu Gln Ser Pro			
50	55	60	

aaa ctg ctg ata tat ggg gca tcc aac cgg tac act ggg gtc ccc gat	240		
Lys Leu Leu Ile Tyr Gly Ala Ser Asn Arg Tyr Thr Gly Val Pro Asp			
65	70	75	80

cgc ttc acg ggc agt gga tct gca aca gat ttc act ctg acc atc agc	288		
Arg Phe Thr Gly Ser Gly Ser Ala Thr Asp Phe Thr Leu Thr Ile Ser			
85	90	95	

agt gtg cag gct gaa gac ctt gca gat tat cac tgt gga cag agt tac	336		
Ser Val Gln Ala Glu Asp Leu Ala Asp Tyr His Cys Gly Gln Ser Tyr			
100	105	110	

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aac tat cca ttc acg ttc ggc tcg ggg aca aag ttg gaa ata aag 381
Asn Tyr Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
115           120          125

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<210> 2
<211> 127
<212> PRT
<213> Mus sp

<220>
<223> AF2 VI

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<400> 2
Met Glu Ser Gln Thr Leu Val Phe Ile Ser Ile Leu Leu Trp Leu Tyr
      1           5           10          15

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Gly Ala Asp Gly Asn Ile Val Met Thr Gln Ser Pro Lys Ser Met Tyr
20 25 30

Val Ser Ile Gly Glu Arg Val Thr Leu Ser Cys Lys Ala Ser Glu Asn
35 40 45

Val Asp Thr Tyr Val Ser Trp Tyr Gln Gln Lys Pro Glu Gln Ser Pro
50 55 60

Lys Leu Leu Ile Tyr Gly Ala Ser Asn Arg Tyr Thr Gly Val Pro Asp
 65 70 75 80

Arg Phe Thr Gly Ser Gly Ser Ala Thr Asp Phe Thr Leu Thr Ile Ser
85 90 95

Ser Val Gln Ala Glu Asp Leu Ala Asp Tyr His Cys Gly Gln Ser Tyr
100 105 110

Asn Tyr Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
115 120 125

<210> 3
<211> 408
<212> DNA
<213> Mus sp.

<220>
<221> CDS
<222> (1) .. (408)
<223> AF2 VH

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<400> 3
atg gga tgg agc tgt atc atc ctc ttc ttg gta gca aca gct aca ggt 48
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
   1          5          10         15

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gtc ctc tcc cag gtc caa ctg cag cag cct ggg gct gac ctt gtg atg   96
Val Leu Ser Gln Val Gln Leu Gln Gln Pro Gly Ala Asp Leu Val Met
          20      25      30

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cct ggg gct cca gtg aag ctg tcc tgc ttg gct tct ggc tac atc ttc 144
 Pro Gly Ala Pro Val Lys Leu Ser Cys Leu Ala Ser Gly Tyr Ile Phe
 35 40 45

acc agc tcc tgg ata aac tgg gtg aag cag agg cct gga cga ggc ctc 192
 Thr Ser Ser Trp Ile Asn Trp Val Lys Gln Arg Pro Gly Arg Gly Leu
 50 55 60

gag tgg att gga agg att gat cct tcc gat ggt gaa gtt cac tac aat 240
 Glu Trp Ile Gly Arg Ile Asp Pro Ser Asp Gly Glu Val His Tyr Asn
 65 70 75 80

caa gat ttc aag gac aag gcc aca ctg act gta gac aaa tcc tcc agc 288
 Gln Asp Phe Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser
 85 90 95

aca gcc tac atc caa ctc aac agc ctg aca tct gag gac tct gcg gtc 336
 Thr Ala Tyr Ile Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val
 100 105 110

tat tac tgt gct aga gga ttt ctg ccc tgg ttt gct gac tgg ggc caa 384
 Tyr Tyr Cys Ala Arg Gly Phe Leu Pro Trp Phe Ala Asp Trp Gly Gln
 115 120 125

ggg act ctg gtc act gtc tct gca 408
 Gly Thr Leu Val Thr Val Ser Ala
 130 135

<210> 4
<211> 136
<212> PRT
<213> Mus sp.

<220>
<223> AF2 VH

<400> 4
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val Leu Ser Gln Val Gln Leu Gln Gln Pro Gly Ala Asp Leu Val Met
 20 25 30

Pro Gly Ala Pro Val Lys Leu Ser Cys Leu Ala Ser Gly Tyr Ile Phe
 35 40 45

Thr Ser Ser Trp Ile Asn Trp Val Lys Gln Arg Pro Gly Arg Gly Leu
 50 55 60

Glu Trp Ile Gly Arg Ile Asp Pro Ser Asp Gly Glu Val His Tyr Asn
 65 70 75 80

Gln Asp Phe Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser
 85 90 95

Thr Ala Tyr Ile Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val
 100 105 110

Tyr Tyr Cys Ala Arg Gly Phe Leu Pro Trp Phe Ala Asp Trp Gly Gln
 115 120 125

Gly Thr Leu Val Thr Val Ser Ala
130 135

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<210> 5  
<211> 384  
<212> DNA  
<213> Artificial Sequence
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<220>
<223> Description of Artificial Sequence:human-mouse
transgenic construct HuZAF VI

<220>
<221> CDS
<222> (1) .. (384)

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<400> 5
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Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
          1           5           10          15

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gga tca acc gga gat att cag atg acc cag tct ccg tcg acc ctc tct 96
Gly Ser Thr Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser
          20      25      30

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gct agc gtc ggg gat agg gtc acc ata acc tgc aag gcc agt gaa aat 144
Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Glu Asn
      35           40           45

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gtg gat act tat gta tcc tgg tat cag cag aag cca ggc aaa gct ccc 192
Val Asp Thr Tyr Val Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
      50           55           60

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aag ctt cta att tat ggg gca tcc aac cgg tac act ggg gta cct tca 240
Lys Leu Leu Ile Tyr Gly Ala Ser Asn Arg Tyr Thr Gly Val Pro Ser
   65          70           75          80

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cgc ttc agt ggc agt gga tct ggg acc gat ttc acc ctc aca atc agc  288
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
          85           90           95

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tct	ctg	cag	cca	gat	gat	ttc	gcc	act	tat	tac	tgc	gga	cag	agt	tac	336
Ser	Leu	Gln	Pro	Asp	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gly	Gln	Ser	Tyr	
100						105					110					

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aac tat cca ttc acg ttc ggt cag ggg acc aag gtg gag gtc aaa cgt 384
Asn Tyr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys Arg
          115           120           125

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<210> 6
<211> 128
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:human-mouse
transgenic construct HuZAF VL

<400> 6
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 1 5 10 15

Gly Ser Thr Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser
 20 25 30

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Glu Asn
 35 40 45

Val Asp Thr Tyr Val Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
 50 55 60

Lys Leu Leu Ile Tyr Gly Ala Ser Asn Arg Tyr Thr Gly Val Pro Ser
 65 70 75 80

Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
 85 90 95

Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Gly Gln Ser Tyr
 100 105 110

Asn Tyr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys Arg
 115 120 125

<210> 7

<211> 409

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:human-mouse
 transgenic construct HuZAF VH

<220>

<221> CDS

<222> (1)..(408)

<400> 7

atg gga tgg agc tgg atc ttt ctc ttc ctc ctg tca ggt acc ggc ggc
 Met Gly Trp Ser Trp Ile Phe Leu Phe Leu Leu Ser Gly Thr Ala Gly
 1 5 10 15 48

gtg cac tct cag gtc cag ctt gtc cag tct ggg gct gaa ctc aag aaa
 Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Leu Lys Lys
 20 25 30 96

cct ggg agc tcc gtg aag gtc tcc tgc aaa gct tct ggc tac atc ttt
 Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe
 35 40 45 144

act agc tcc tgg ata aac tgg gta aag cag gcc cct gga cag ggt ctc
 Thr Ser Ser Trp Ile Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu
 50 55 60 192

gag tgg att gga agg att gat cct tcc gat ggt gaa gtt cac tac aat
 Glu Trp Ile Gly Arg Ile Asp Pro Ser Asp Gly Glu Val His Tyr Asn
 65 70 75 80 240

caa gat ttc aag gac aag gct aca ctt aca gtc gac aaa tcc acc aat 288
 Gln Asp Phe Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Thr Asn
 85 90 95

aca gcc tac atg gaa ctg agc ctg aga tca gag gac act gca gtc 336
 Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
 100 105 110

tat tac tgt gca aga gga ttt ctg ccc tgg ttt gct gac tgg ggc caa 384
 Tyr Tyr Cys Ala Arg Gly Phe Leu Pro Trp Phe Ala Asp Trp Gly Gln
 115 120 125

gga acc ctg gtc aca gtc tcc tca g 409
 Gly Thr Leu Val Thr Val Ser Ser
 130 135

<210> 8
<211> 136
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:human-mouse
transgenic construct HuZAF VH

<400> 8
Met Gly Trp Ser Trp Ile Phe Leu Phe Leu Leu Ser Gly Thr Ala Gly
 1 5 10 15

Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Leu Lys Lys
 20 25 30

Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe
 35 40 45

Thr Ser Ser Trp Ile Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu
 50 55 60

Glu Trp Ile Gly Arg Ile Asp Pro Ser Asp Gly Glu Val His Tyr Asn
 65 70 75 80

Gln Asp Phe Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Thr Asn
 85 90 95

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ala Arg Gly Phe Leu Pro Trp Phe Ala Asp Trp Gly Gln
 115 120 125

Gly Thr Leu Val Thr Val Ser Ser
 130 135

<210> 9
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:humanized
immunoglobulin huZAF

<400> 9
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Leu Lys Lys Pro Gly Ser
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Ser Ser
20 25 30
Trp Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45
Gly Arg Ile Asp Pro Ser Asp Gly Glu Val His Tyr Asn Gln Asp Phe
50 55 60
Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Thr Asn Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Gly Phe Leu Pro Trp Phe Ala Asp Trp Gly Gln Gly Thr Leu
100 105 110
Val Thr

<210> 10
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:humanized
immunoglobulin huZAF

<400> 10
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Leu Lys Lys Pro Gly Ser
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Ser Ser
20 25 30
Trp Ile Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45
Gly Arg Ile Asp Pro Ser Asp Gly Glu Val His Tyr Asn Gln Asp Phe
50 55 60
Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Thr Asn Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Phe Leu Pro Trp Phe Ala Asp Trp Gly Gln Gly Thr Leu
 100 105 110

Val Thr

<210> 11
 <211> 114
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:humanized
 immunoglobulin haf25

<400> 11
 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Ser Ser
 20 25 30

Trp Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Arg Ile Asp Pro Ser Asp Gly Glu Val His Tyr Asn Gln Asp Phe
 50 55 60

Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Thr Asn Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Gly Phe Leu Pro Trp Phe Ala Asp Trp Gly Gln Gly Thr Leu
 100 105 110

Val Thr

<210> 12
 <211> 107
 <212> PRT
 <213> Homo sapiens

<220>
 <223> Variable region of the human Eu antibody light
 chain.

<400> 12
 Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Asn Thr Trp
 20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Met
 35 40 45

Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ile Gly
 50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Asp Ser Lys
 85 90 95

Met Phe Gly Gln Gly Thr Lys Val Glu Val Lys
 100 105

<210> 13
<211> 117
<212> PRT
<213> Homo sapiens

<220>
<223> Variable region of the human Eu antibody heavy
chain.

<400> 13
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Arg Ser
 20 25 30

Ala Ile Ile Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Gly Ile Val Pro Met Phe Gly Pro Pro Asn Tyr Ala Gln Lys Phe
 50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Phe Tyr Phe Cys
 85 90 95

Ala Gly Gly Tyr Gly Ile Tyr Ser Pro Glu Glu Tyr Asn Gly Gly Leu
 100 105 110

Val Thr Val Ser Ser
 115